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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,853	06/24/2003	Yung-Nien Chang	105576-0065-101	9278

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/602,853	CHANG ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-96* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Terminal Disclaimers, filed 9 February 2009.

Claim Status

Claims 38-96 are pending. No amended claims have been submitted. Claims 38-96 are under current examination.

Priority

This application claims benefit as a DIV of 08/974,391 (filed 11/19/1997; issued as US PAT 6,638,762) which is a CIP of 08/487,992 (filed 06/07/1995 ABN) which is a CIP of 08/348,258 (filed 11/28/1994 ABN) and said 08/974,391 (filed 11/19/1997) which is a CIP of 08/849,117 (filed 08/01/1997; issued as US PAT 5,998,205) which is a 371 of PCT/US95/15455 (filed 11/28/1995) which is a CIP of 08/487,992 (filed 06/07/1995 ABN) which is a CIP of 08/348,258 (filed 11/28/1994 ABN).

It has been determined that the pending claims contain limitations which require the use of a tissue specific promoter to express heterologous sequences/therapeutic sequences in the adenoviral vector. The first support for these limitations is in the original claims of specification 08/974,391 (filed 11/19/1997; issued as US-6,638,762). Therefore, the effective filing date of this application because of these newly introduced limitations is the filing date of application 08/974,391.

Therefore, the instant application has been granted the benefit date, 19 November 1997, from the filing date of the application, 08/974,391.

Terminal Disclaimer

The terminal disclaimers filed on 2/9/2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US-5998205, US-6551587, US-6638762, and any patent granted on US applications 11/601071, 11/977902, and 11/977533 has been reviewed and is accepted. The terminal disclaimer has been recorded.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 38-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson et al., et al., (US Patent No. 5,698,443) in view of Woo et al., (US Patent No. 5,631,236.

The claims are readable on a virion comprising an expression adenovirus vector and a cell comprising a first coding sequence operably linked to a tissue-specific promoter wherein the gene product of the first coding sequence is essential for vector replication, and a second heterologous gene sequence encoding a gene product with anti-tumor activity in the cells.

Henderson et al., teach an adenovirus vector comprising an adenovirus early gene essential for replication under the transcriptional control of a regulatory sequence, said regulatory sequence comprising an enhancer and promoter specific for control by prostate cancer cells, for expression of a prostate specific antigen (claim 1; column 3, lines 2-17). Additionally, Henderson discloses an adenovirus vectors comprising at least one of the genes E1A, E1B or E4 and a transgene under the transcriptional control of a prostate cell specific response element (claims 5-7). Henderson further teaches that is routine in the art to employ transcriptionally initiation regions that are only transcriptionally active in the target cells of interest for replication of competent

adenovirus vectors, where a transgene (e.g., heterologous gene) under a cell specific promoter may also be present (col. 2, 54-61). Additionally, Henderson describes that the adenovirus vector is a vehicle for introducing new genetic capability, particularly associated with cytotoxicity for treating neoplasia (e.g. cancerous cell) (col. 6, 25-34).

Henderson et al., do not specifically teach other tissue specific promoters such as alpha-fetoprotein and erb-B2.

However, at the time the invention was made, Woo et al., (US Patent No. 5,631,236) is exemplified art that teaches delivering of a recombinant adenoviral vector containing the herpes simplex virus-thymidine kinase gene under the control of tissue specific promoters for effective treatment of localized solid tumors and papilloma (col. 1, lines 6-11). Moreover, Woo et al., discloses in Table II a list of tissue specific promotes that are well known in the art at the time the invention was made including Erb-B2 (e.g., for breast and G.I. delivery) alpha fetoprotein (e.g., for liver delivery).

Therefore, it would have been obvious for one of ordinary skill in the art to have employed any of the known tissue specific promoters including Erb-B2 and alpha fetoprotein as exemplified by Woo et al., in the vector taught by Henderson in order to target expression of a gene of interest in a cell with a reasonable expectation of success, particularly since Henderson teaches the advantage of using a replication competent vector containing a tissue specific promoter operably linked to a coding sequence essential to adenoviral replication. Thus, one of ordinary skill in the art would have been motivated to have employed any of the known specific promoters, including Erb-B2 (e.g., for breast and G.I. delivery) alpha fetoprotein (e.g., for liver delivery), as

exemplified by Woo et al., in the vector taught by Henderson in order to enhance expression of a gene of interest in a cell.

Therefore the virion as taught by Henderson et al. in view of Woo et al. would have been *prima facie* obvious over the virion of the instant application.

Claims 38-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson et al., et al., (US Patent No. 5,698,443) in view of Abe et al., (PNAS, 90:282-286, 1993; IDS 6/24/2003, item AR).

The claims are readable on a virion comprising an expression adenovirus vector and a cell comprising a first coding sequence operably linked to a tissue-specific promoter wherein the gene product of the first coding sequence is essential for vector replication, and a second heterologous gene sequence encoding a gene product with anti-tumor activity in the cells.

Henderson et al., teach an adenovirus vector comprising an adenovirus early gene essential for replication under the transcriptional control of a regulatory sequence, said regulatory sequence comprising an enhancer and promoter specific for control by prostate cancer cells, for expression of a prostate specific antigen (claim 1; column 3, lines 2-17). Additionally, Henderson discloses an adenovirus vectors comprising at least one of the genes E1A, E1B or E4 and a transgene under the transcriptional control of a prostate cell specific response element (claims 5-7). Henderson further teaches that is routine in the art to employ transcriptionally initiation regions that are only

transcriptionally active in the target cells of interest for replication of competent adenovirus vectors, where a transgene (e.g., heterologous gene) under a cell specific promoter may also be present (col. 2, 54-61). Additionally, Henderson describes that the adenovirus vector is a vehicle for introducing new genetic capability, particularly associated with cytotoxicity for treating neoplasia (e.g. cancerous cell)(col. 6, 25-34).

Henderson et al., do not specifically teach other tissue specific promoters such as DF3.

However, at the time the invention was made, Abe et al., is exemplified art that teaches the promoter region regulating transcription of the DF3 gene in human MCF-7 breast cancer cells (p. 282, col. 1) .

Therefore, it would have been obvious for one of ordinary skill in the art to have employed any of the known tissue specific promoters including DF3 as exemplified by Abe et al., in the vector taught by Henderson in order to target expression of a gene of interest in a cell with a reasonable expectation of success, particularly since Henderson teaches the advantage of using a replication competent vector containing a tissue specific promoter operably linked to a coding sequence essential to adenoviral replication. Thus, one of ordinary skill in the art would have been motivated to have employed any of the known specific promoters, including DF3, as exemplified by Abe, in the vector taught by Henderson in order to enhance expression of a gene of interest in a cell.

Therefore the virion as taught by Henderson et al. in view of Abe et al. would have been *prima facie* obvious over the virion of the instant application.

Claims 38-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson et al., et al., (US Patent No. 5,698,443) in view of Smith et al., (Human Gene Therapy 5:29-35, 1994; IDS submitted 6/24/2003, item AA)

The claims are readable on a virion comprising an expression adenovirus vector and a cell comprising a first coding sequence operably linked to a tissue-specific promoter wherein the gene product of the first coding sequence is essential for vector replication, and a second heterologous gene sequence encoding a gene product with anti-tumor activity in the cells.

Henderson et al., teach an adenovirus vector comprising an adenovirus early gene essential for replication under the transcriptional control of a regulatory sequence, said regulatory sequence comprising an enhancer and promoter specific for control by prostate cancer cells, for expression of a prostate specific antigen (claim 1; column 3, lines 2-17). Additionally, Henderson discloses an adenovirus vectors comprising at least one of the genes E1A, E1B or E4 and a transgene under the transcriptional control of a prostate cell specific response element (claims 5-7). Henderson further teaches that is routine in the art to employ transcriptionally initiation regions that are only transcriptionally active in the target cells of interest for replication of competent adenovirus vectors, where a transgene (e.g., heterologous gene) under a cell specific promoter may also be present (col. 2, 54-61). Additionally, Henderson describes that

the adenovirus vector is a vehicle for introducing new genetic capability, particularly associated with cytotoxicity for treating neoplasia (e.g. cancerous cell)(col. 6, 25-34).

Henderson et al., do not specifically teach other tissue specific promoters such as surfactant promoter.

However, at the time the invention was made, Smith et al., is exemplified art that teaches the promoter region regulating transcription of the human surfactant protein A (SPA) gene in non small cell lung cancers (NSCLC) (p. 29, col. 1) .

Therefore, it would have been obvious for one of ordinary skill in the art to have employed any of the known tissue specific promoters including surfactant as exemplified by Smith et al., in the vector taught by Henderson in order to target expression of a gene of interest in a cell with a reasonable expectation of success, particularly since Henderson teaches the advantage of using a replication competent vector containing a tissue specific promoter operably linked to a coding sequence essential to adenoviral replication. Thus, one of ordinary skill in the art would have been motivated to have employed any of the known specific promoters, including surfactant, as exemplified by Smith, in the vector taught by Henderson in order to enhance expression of a gene of interest in a cell.

Therefore the virion as taught by Henderson et al. in view of Smith et al. would have been *prima facie* obvious over the virion of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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